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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/548,883	04/13/2000	Michael I. Watkins	2558B-061300US	7641

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	12

DATE MAILED: 09/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/548,883	WATKINS ET AL.	
	Examin r	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 5/20/02 in Paper No. 10 is acknowledged and has been entered. Claim 1 has been amended. Claims 1-25 are pending. Currently, claims 1-22 are under examination

Rejections Maintained ~~withdrawn~~

2. In light of Applicant's argument, the rejection of claims 4-5 under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824) as applied to claims 1-2, 7-15, and 18-19 above, and further in view of Evans et al. (US 5,071,773), is hereby, withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-22 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step a), as amended, is vague and indefinite in reciting, "distinguishable characteristic that is *independent* of the coatings of i), ii), iii), and iv), i.e. immobilized specific antibodies, because it is unclear, how simultaneous (multiplex) analyte determination, as required by the preamble is achieved if the coating is "independent" from what is defined by, or is not representative of the particular set of the particles.

Claim 1, step c) is vague and indefinite in reciting, "detecting the amount of label bound to said particles" and "correlating ... the amount of label thus detected to the group to which said label is bound" because it is unclear, as recited, how the label binds specifically to the particle. Perhaps, Applicant intends "detecting the amount of labeled antibodies that bound to their respective analytes that have been previously captured by immobilized corresponding antibodies that are coated into particles". Thus, it is the complex formed by the immobilized (capture) antibody - analyte - labeled antibody that is being flow cytometrically detected and measured. See also claim 12.

Accordingly, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claims stand on their own merit.

Claim 12 is ambiguous in reciting, "said particles incorporate dyes" because it appears that the particles intend to incorporate dyes, as part of the method step. Perhaps Applicant intends that "said particles have specific dye or dyes incorporated thereto".

Claim 20 remains indefinite in reciting, "useful" because the term "useful" is a subjective term that lacks a comparative basis for defining its metes and bounds. See

also claims 21-22. Perhaps, Applicant intends, "provides a substantially greater sensitivity in measuring lower concentrations lower of ..."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2, 7-15, and 18-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824) for reasons of record.

Watkins et al. disclose a multiplex flow assay for analyzing a single patient sample to simultaneously determine biological markers indicative of thyroid function or disorders (see column 3, lines 6-26). According to Watkins et al., multiple combination assays can be performed on the single patient sample; thus combining competitive, sandwich, immunometric, and serological assays such as assays for thyroid stimulating hormone (TSH) and free thyroxine (T_4) or total T_4 (see column 9, lines 27-34). Specifically, Watkins et al. disclose incubating the sample with a mixture of solid phase particles in a suspension having anti-TSH antibody coated thereto. Simultaneously or sequentially, the sample is recovered and further incubated with a second anti-TSH antibody that binds another epitope of TSH which is conjugated with a label, i.e.

phycoerythrin (see column 8, lines 33-52). Watkins et al. disclose that the solid phase particles may be provided in different groups wherein each group has different antibodies immobilized thereto; i.e. these antibodies in each group are specific to the different immunoglobulin classes such as anti-IgM antibodies and anti-IgG antibodies (see column 10, lines 20-60). Watkins et al. specifically use solid magnetic particles as solid phase which are classifiable by flow cytometry into discrete groups according to distinguishable characteristics, differentiation parameters, and specific antibodies or antigens (assay reagents) which bind in a selective manner (see column 3, lines 6-27 and column 7, line 65 to column 8, line 6). Differentiation parameters include size, fluorescence labels, angle scatter, light emission, density, absorbance, and number of particles for each group (see columns 6-7). The solid particles comprise magnetically responsive materials wherein recovery of these materials after incubation is achieved by subjecting the suspensions to magnetic field to cause the particles to adhere to a reaction vessel wall (see column 3, lines 28-37 and column 8, lines 11-32). Each solid particle group has a fluorescein dye incorporated thereto at differing concentrations and the assay specific antibodies or antigens are labeled with phycoerythrin (see column 6, lines 40-52).

Watkins et al. differ from the instant invention in failing to disclose further assaying the patient sample for triiodothyronine (T_3) and human thyroid peroxidase (hTPO) as biological markers in determining thyroid disorder or function.

Dietzen discloses that a full understanding of thyroid function requires accurate assessment of the amounts of TSH, T_3, and T_4. Dietzen, therefore, provides a standard

solution which contains specific amounts of TSH, T_3, and T_4 for use in simultaneous multiple thyroid related-analyte binding assays (see column 2, lines 56-67). The standard also contains serum bovine albumin as the binding protein or diluting agent for the standard (see column 5, lines 15-41). According to Dietzen, large glycoproteins such as TSH are measured by two-site sandwich immunoassay technology, i.e. using anti-TSH antibodies as capture and detection antibodies. Smaller molecules at smaller concentrations such as T_3 and T_4 are determined by competitive hapten immunoassay using anti-T_3 antibodies and anti-T_4 antibodies (see column 6).

Weckermann et al. disclose that human thyroid peroxidase (hTPO) is a glycosylated hemopoietin which is bound to thyroid membranes and performs an important function in the biosynthesis of thyroid hormones (see page 1, paragraph 2). The hTPO is identical to a microsomal antigen which is recognized as autoantigen of circulating anti-thyroid antibodies, i.e. anti-hTPO, (autoantibodies) which are detected in patients having autoimmune disease of the thyroid. These anti-thyroid antibodies, thus, play an important role as biological markers in assessing thyroid function or disorder (see page 2). Weckermann et al. disclose immobilizing monoclonal anti-hTPO antibodies into solid phase particles and labeling anti-hTPO antibodies for use as binding partners in a sandwich assay for quantitative determination of hTPO. The first mAb is specific for a region of the hTPO that is involved in binding of autoantibodies against hTPO. Alternatively, Weckermann et al. disclose preparing standards comprising hTPO from human thyroid membranes which are purified by affinity chromatography for use in binding assay with anti-hTPO antibodies (see page 11, lines

27-30). Recombinant hTPO is also commercially available in a buffer solution (see page 12, lines 1-8).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Dietzen and Weckerman in assaying for T_3 and hTPO with the multiplex method for assaying TSH and T_4 utilizing groups of identifiable particles, i.e. beads, as taught by Watkins because Watkins specifically taught that his method allows for simultaneous multiple determination and differentiation of physiologically related analytes such as TSH, T_4, T_3, and hTPO which are all analytes that can provide individually and cumulatively, an assessment of thyroid function.

Watkins, Dietzen, and Weckermann have been discussed supra. Watkins, Dietzen, and Weckermann does not teach that hTPO can be coated to particles at a density of 0.3 ng/cm^2 to about 1.0 µg/cm^2 and at a density of 0.5 ng/cm^2 to about 50 ng/cm^2 in claims 18 and 19.

It is, however, maintained that parameters, i.e., density coating of 0.3 ng/cm^2 to about 1.0 µg/cm^2 and 0.5 ng/cm^2 to about 50 ng/cm^2 are all differentiation parameters comprising result effective variables which Watkins has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process

by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 18-19 are for any particular purpose or solve any stated problem and the prior art teaches that differentiation parameters often vary according to the reagent being used or sample being assayed, solutions and parameters utilized by Watkins appear to work equally as well. Therefore, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the method disclosed by the Watkins by normal optimization procedures.

5. Claims 20-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824) as applied to claims 1-2, 7-15, and 18-19 above, and further in view of Frengen (US 5,723,346) for reasons of record.

Watkins, Dietzen, and Weckermann have been discussed supra. Watkins, Dietzen, and Weckermann differ from the claimed invention in failing to disclose use of two subgroups differing in particle size and/or coating density so as to provide greater sensitivity for lower concentrations of TSH.

Frengen discloses a binary assay method capable of providing a wide dynamic range and a high degree of precision wherein two subgroups of particles differing from each other in particle size and coating density, i.e. diameter, composition, reactive

surface groups, are used (see column 3, lines 47-55 and column 6). Specifically, Frengen discloses reacting a sample with a first binding partner having affinity for a biological marker, i.e. thyroid function marker, a labeled ligand having affinity for the marker, a second binding partner having affinity for the labeled ligand, wherein the first and the second binding partners are independently distinguishable and determinable particle forms and the marker concentrations obtained therefrom are determined using a standard curve (see column 3, lines 56-67).

One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the binary assay using two distinguishable particles taught by Frengen into the multiplex assay method as taught by Watkins because Frengen specifically taught that incorporating binary systems into sandwich assays such as the TSH assay of Watkins provides for a wider or broader dynamic range, particularly in high analyte concentrations wherein the dynamic range would, otherwise, be limited by a phenomenon called hook effect which is usually seen in increased amounts of analyte .

6. Claims 3 and 16-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824) as applied to claims 1-2, 7-15, and 18-19 above, and further in view of Smith et al. (US 4,332,784) for reasons of record.

Watkins et al., Dietzen, and Weckermann have been discussed supra. Watkins et al., Dietzen, and Weckermann differ from the instant invention in failing to disclose

further assaying the patient sample for anti-thyroglobulins as biological markers in determining thyroid disorder or function.

Smith et al. disclose dual isotope assays for assessing thyroid function or disorder. Smith et al. disclose carrying out an assay for two of TSH, T_3, T_4, and thyroxine binding globulins or thyroglobulin (TBG) which play an important role as biological markers in assessing thyroid function or disorder (see Abstract). Smith et al. disclose an assay for determining T_3 and T_4 using anti-T_4 and anti-T_3 antibodies as immunological binding partners in Example 4, TSH and T_4 using anti-T_4 antibodies and anti-TSH antibodies as immunological binding partners in Example 5, and T_4 and TBG using anti- T_4 and anti-TBG antibodies as immunological binding partners to react and bind T_4 and TBG in Example 6 (see columns 7-8). Smith et al. also use human serum with calibrated T_4 and TBG levels as standards. Smith et al. disclose adding a solution containing 20% w/v polyethylene glycol (PEG) as a solute in the suspension with the binding components to terminate reaction and precipitate bound components in the assay reaction (see column 7, lines 1-6).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Smith in assaying for anti-TBG with the multiplex method for assaying TSH and T_4 utilizing groups of identifiable particles, i.e. beads, as taught by Watkins and modified by Dietzen and Weckerman by additionally assaying for T_3 and hTPO, because Watkins specifically taught that his method allows for simultaneous multiple determination and differentiation of physiologically related

analytes such as TSH, T_4, T_3, hTPO, and TBG which are all analytes that can provide individually and cumulatively, an assessment of thyroid function.

Watkins, Dietzen, Weckermann, and Smith have been discussed supra. Watkins, Dietzen, Weckermann, and Smith do not teach concentrations of 0.5% to about 4.0% by weight of PEG in claim 16 and 2.0% to about 3.0% by weight of PEG in claim 17.

It is, however, maintained that parameters, i.e., solute concentrations in assay reagents and buffers, comprise result effective variables which Smith has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 16 and 17 are for any particular purpose or solve any stated problem and Smith teaches that concentration of PEG often vary according to reagent usage, concentration parameters of PEG utilized by Smith appear to work equally as well. Therefore, absent unexpected results, it would have been obvious for one of ordinary

skill to discover the optimum workable ranges of the method disclosed by the Smith by normal optimization procedures.

7. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watkins et al. (US 6,280,618) in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824) as applied to claims 1-2, 7-15, and 18-19 above, and further in view Frieden et al. (J. Biol. Chem. (1948), 176, 155-63) and Block et al. (J. Med. Chem. (1976), 19(8), 1067-9).

Watkins et al., Dietzen, and Weckermann have been discussed supra. Watkins et al., Dietzen, and Weckermann differ from the instant invention in failing to disclose an analog composition which is a single species having immunological binding to both anti-triiodothyronine and anti-thyroxine.

Frieden et al. specifically teach that certain thyroxine analogs such as N-acetyl-3,5-diiodo-L-tyrosine previously synthesized by Myers (1932), exhibit physiological thyroxine-like activity and are structurally related as competitive inhibitors for thyroxine.

Block et al. teach synthesizing 3-iodo-L-thyronine and its iodinate derivatives including N-acetyl-3-iodo-L-tyrosine.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute thyroxine analogs such as N-acetyl-3,5-diiodo-L-tyrosine as taught by Frieden or N-acetyl-3-iodo-L-tyrosine as taught by Block, for the binding members comprising anti-triiodothyronine and anti-thyroxine in the method of Watkins as modified by Dietzen and Weckermann, because Frieden specifically taught

that thyroxine analogs are structurally related as competitive inhibitors for thyroxine and Watkins and Dietzen are generic with the type of immunological binding partners used for T_3 and T_4 in their competitive assays. Further, the N-acetyl-3-iodo-L-tyrosine as synthesized by Block constitutes an obvious modification of thyroxine analogs which are routinely varied in the art and which have not been described as being critical to the practice of the invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,280,618 in view of Dietzen (US 5,795,789) and in further view of Weckermann (WO 95/02824) and Smith et al. (US 4,332,784).

Patent No. 6,280,618 discloses a multiplex flow assay for simultaneously detecting and analyzing a plurality of analytes in a single patient sample (see column 3, lines 6-26). Multiple combination assays can be performed on the single patient sample; thus combining competitive, sandwich, immunometric, and serological assays such as assays, i.e. for thyroid stimulating hormone (TSH) and free thyroxine (T_4) or total (T_4) (see column 9, lines 27-34). The sample is incubated with a mixture of solid phase particles in a suspension having a reagent coated thereto. The sample is further incubated with a labeled antibody that binds another epitope of the analyte; thus labeled antibody (see column 8, lines 33-52). Patent No. 6,280,618 specifically uses solid magnetic particles as solid phase which are classifiable by flow cytometry into discrete groups according to distinguishable characteristics, differentiation parameters, and specific antibodies or antigens (assay reagents) which bind in a selective manner (see column 3, lines 6-27 and column 7, line 65 to column 8, line 6). Differentiation parameters include size, fluorescence labels, angle scatter, light emission, density, absorbance, and number of particles for each group (see columns 6-7). The solid

particles comprise magnetically responsive materials wherein recovery of these materials after incubation is achieved by subjecting the suspensions to magnetic field to cause the particles to adhere to a reaction vessel wall (see column 3, lines 28-37 and column 8, lines 11-32). Each solid particle group has a fluorescein dye incorporated thereto at differing concentrations and the assay specific antibodies or antigens are labeled with phycoerythrin (see column 6, lines 40-52).

Patent No. 6,280,618 differs from the instant invention in failing to disclose assaying the patient sample specifically for TSH, T_3, T_4, and hTPO as biological markers in determining thyroid disorder or function.

Dietzen discloses that a full understanding of thyroid function requires accurate assessment of the amounts of TSH, T_3, and T_4. Dietzen, therefore, provides a standard solution which contains specific amounts of TSH, T_3, and T_4 for use in simultaneous multiple thyroid related-analyte binding assays (see column 2, lines 56-67). The standard also contains serum bovine albumin as the binding protein or diluting agent for the standard (see column 5, lines 15-41). According to Dietzen, large glycoproteins such as TSH are measured by two-site sandwich immunoassay technology, i.e. using anti-TSH antibodies as capture and detection antibodies. Smaller molecules at smaller concentrations such as T_3 and T_4 are determined by competitive hapten immunoassay using anti-T_3 antibodies and anti-T_4 antibodies (see column 6).

Weckermann et al. disclose that human thyroid peroxidase (hTPO) is a glycosylated hemopoietin which is bound to thyroid membranes and performs an important function in the biosynthesis of thyroid hormones (see page 1, paragraph 2).

The hTPO is identical to a microsomal antigen which is recognized as autoantigen of circulating anti-thyroid antibodies, i.e. anti-hTPO, (autoantibodies) which are detected in patients having autoimmune disease of the thyroid. These anti-thyroid antibodies, thus, play an important role as biological markers in assessing thyroid function or disorder (see page 2). Weckermann et al. disclose immobilizing monoclonal anti-hTPO antibodies into solid phase particles and labeling anti-hTPO antibodies for use as binding partners in a sandwich assay for quantitative determination of hTPO. The first mAb is specific for a region of the hTPO that is involved in binding of autoantibodies against hTPO. Alternatively, Weckermann et al. disclose preparing standards comprising hTPO from human thyroid membranes which are purified by affinity chromatography for use in binding assay with anti-hTPO antibodies (see page 11, lines 27-30). Recombinant hTPO is also commercially available in a buffer solution (see page 12, lines 1-8).

Smith et al. disclose dual isotope assays for assessing thyroid function or disorder. Smith et al. disclose carrying out an assay for two of TSH, T_3, T_4, and thyroxine binding globulins or thyroglobulin (TBG) which play an important role as biological markers in assessing thyroid function or disorder (see Abstract). Smith et al. disclose an assay for determining T_3 and T_4 using anti-T_4 and anti-T_3 antibodies as immunological binding partners in Example 4, TSH and T_4 using anti-T_4 antibodies and anti-TSH antibodies as immunological binding partners in Example 5, and T_4 and TBG using anti- T_4 and anti-TBG antibodies as immunological binding partners to react and bind T_4 and TBG in Example 6 (see columns 7-8). Smith et al. also use human serum

with calibrated T_4 and TBG levels as standards. Smith et al. disclose adding a solution containing 20% w/v polyethylene glycol (PEG) as a solute in the suspension with the binding components to terminate reaction and precipitate bound components in the assay reaction (see column 7, lines 1-6).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Dietzen and Weckerman in assaying for TSH, T_3, T_4, hTPO, and TBG into the method taught in US Patent No. 6,280,618 to assay thyroid function because Patent No. 6,280,618 specifically taught that the method allows for simultaneous multiplex analyte determination and differentiation of physiologically related analytes such as in the case of thyroid function analytes: TSH, T_4, T_3, hTPO, and TBG.

Response to Arguments

9. Applicant's arguments filed 5/20/02 have been fully considered but they are not persuasive.

A) Applicant argues that claim 1, step c) is clear and definite and thoroughly explains how "the label bound to the particles".

In response, it is noted that the features upon which applicant relies upon for argument purposes are not recited in the rejected claim. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

B) Applicant argues that Watkins et al. '618 is improperly cited as prior art because the '618 patent qualifies only under subsection e) of section 102 since its issue date postdates the filing of the present application and names different inventors. Applicant argues that the '618 patent and the present application are commonly owned by the same assignee, Bio-Rad Laboratories, Inc, and the present application is established by the assignment recorded at the USPTO on December 19, 2000.

In response, Applicant's argument is not persuasive because Applicant fails to provide the required evidence in the form of a statement *that the application and the reference were, at the time the invention was made, owned by, or subject to an obligation of assignment to, the same person.* Assignment records by themselves, i.e. without the required statement by Applicant, are not sufficient evidence since assignment records do not show the required "at the time the invention was made" statement.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
September 17, 2002

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641